

ISTITUTO DI GENETICA UNIVERSITÀ DI PAVIA VIA SANT'EPIFANIO, 14 27100 PAVIA 9 June 1970

Prof. Joshua Lederberg Stanford University School of Medicine Palo Alto, California U.S.A.

Dear Joshua,

I was very pleased with the contents of your letter re the computer statistics course. I apologize for not writing to Bill Brown directly and I hope you will pass to him the relevant part of this letter. It was indeed good news that the computer Statistics course was a success and I hope Bill and Bruce will continue on it. I am especially interested in Bill's suggestion of expanding the course into two quarters, and on the possibility that the second quarter might be used in pard as a laboratory for my population biology course. I am also greatly interested that they continue experimenting with this method of teaching statistics and will be happy to collaborate in any way — more so, perhaps, in the planning, than in the actual teaching, because of my other commitments in teaching. Maybe we will sometime be able to write a book on this jointly with Bill and/or Bruce!

for a short writ I am not yet aware of when I will be able to come to Stanford, so that it may be useful to start some planning by correspondence. Naturally, it would greatly help me to know something more on the course that was given this year: line, if available, as well as projects for the course when it will double its present size. I can make some very tentative suggestions on the possible partition of the subject into two courses, that will also help to take into consideration needs for the population biology course. Timing is an important consideration. If my course has to be given in the Spring term, which would be best (I could also give it in the Winter 1970, but it would be somewhat inconvenient), then the first course of statistics should be given in the Winter term, and the second one in parallel with the population biology course in the Spring Alternative solutions could be found. Thus, Computer Statistics part I could take place in the Fall, Computer Statistics part II in the Winter, and Population Biology in the Spring. In the latter case it would be important to be able to offer the chance of some computer work to students of the Population

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Biology in the second quarter, but it is a solution which is more demanding in terms of students' time.

I wonder how far the following suggested outlines are compatible with this year's experience, and the needs of the medical students:

Computer Statistics I. Use of computers for elementary or ready-made programs. Random numbers, Random sampling, means of measures of diffusion, Binomial distribution, Normal, Poisson, Standard sampling distributions and their applications in significance testing: t, chi square, F in the simplest types of analysis of variance. The use of the correlation coefficient and simple regression. The computer should help in providing, by simulation, a clearer grasp of the fundamental distributions, binomial, normal, and Poisson, and the sampling distributions. It would be important to give in this or in the next course the essentials of experimental design.

Computer Statistics II. Elements of matrix algebra. Multiple regression and correlation. Maximum likelihood estimation. Discriminant analysis. Principal components. Other advanced statistical methods, including perhaps analysis of time series, numerical taxonomy, etc. An essential aspect of this course should perhaps be that of allowing the student considerable freedom in the choice of problems, so as to suit his special interests, but guaranteeing constant expert supervision both for computing problems and for interpretation of potential and meaning of methods. Students should be encouraged to use simulation as a method in problem solving, when mathematical theory is inadequate.

It might be useful if I give some ideas of the type of problems which might be given to students of Population Biology as laboratory problems:

- 1) testing a Hardy-Weinberg equilibrium in some simple cases. This can be done by desk computer also, but it could be easily programmed by the student.
- 2) construction of selection curves by applying the recurrence formulas, giving values of gene or genotype frequencies from one generation to the next, which are simple and exact. A simple program might be used for various types of selection: for and against heterozygotes, with varying intensities of selection, etc. The students might write the program themselves (eight to ten instructions are sufficient). I wrote many of these programs to build the figures in the book with Walter.

- 3) population projection by the matrix method, to show how fast Lotka's stable age distribution is reached, and to give a feeling of population growth and how mortality and fertility affect it.
- 4) random genetic drift by simulation. There is a very simple example of a program to do this in the appendix of our book. Programs could be written by the students.
- 5) simulation of more complex situations involving drift, mutation, selection. This may be relatively complex, and existing programs might be used.
- 6) simulation of a genetic trait due to several genes and influenced by the environment: effects on correlations between relatives of varying degrees. This is a complex program. It might be written as a joint effort by the students.
- 7) Use of standard programs for estimation of gene frequencies, segregation, linkage, etc.

It may not be easy to fit all these exercises into a course designed for something else, unless computer course II is fairly flexible. I believe it is not absolutely essential to make this course compulsory for the population biology students: they may get enough from formulas and graphs. But it can certainly be stimulating and add a great deal to true understanding. It would be useful also for medical students who want to increase their understanding of the human genetics course.

The above are tentative suggestions. I am not entirely satisfied with them and look forward to reactions from you, Bill, and Bruce. Mark, if at Stanford, might be useful in helping with the course. As it may help to plan my own course to know what will be available from the statistical point of view, I am doubly interested in corresponding on the matter.

Population Biology course. From what I understand, my course should come after Pittendrigh's course, and as part of Ehrlich's course or, better as an independent course (title: Human Population Genetics?) I think it would be better if it were separate, because it might then be used also by some medical students as a complement or as an alternative to what they get at present.

In order to avoid repetitions, it would be essential to have detailed outlines of what will have been done by others. Apart from repetitions to be avoided which I am unable to foresee at the moment, the course could probably be close to what there is in the book with Walter, the contents of which in short are: 1) Mendelian equilibria (Mardy Weinberg); 2) abundance and fate of deleterious mutations in man including chromosomal ones; 3) selection for favorable mutants and for heterozygosis; 4) incompatibility and polymorphisms connected with it; 5) demography and natural selection; 6) consanguineity and inbreeding; 7) drift, migration, gene flow; 8) quantitative traits, threshold traits, interaction of genotype and environment; 9) the geneticist's point of view on human races and the human species; 10) a general picture of the forces affecting evolution in man; 11) eugenics and euphenics.

Much of point 11 (Euphenics) would be in your own course.Other possible repetitions to be avoided: e.g. in course 3a, "development of human races" is indicated. If this refers to "growth" then there is no duplication problem. If it refers to genetics then there my be an overlap with point 9 above. Another possible overlap is with respect to demography. How much demography should the students have? My own background is rather inadequate to give the kind of details of which demographers are usually so greedy. I am also a little impatient with thi type of demography. Of the more general aspects of demography I have only a superficial knowledge, but there are only few demographers, as far as I am aware (e.g. Keyfitz at Berkeley, Coale at Princeton) who really know this kind of demography. I am not convinced it is necessary to give a full course in demography to all students, but some may want to take one. My tendency would be to give only two or three lectures on this topic. One practical problem listed before (number 3) exemplifies this. It is based on a recent method by Keyfitz which we have used in our book, and can give a grasp of the relationship between mortality, fertility, and population increase as well as age distribution. This is really the central problem and I would tend to be content with it, also because it is important to master it in order to understand fully the consequencies of natural selection. But students should be given the option of learning more about demography from somebody who really knows it.

I am puzzled by the title "Population Biology" and am wondering how many things that should go under this name are not covered in the course I or other people might give under the same title. I hope you will expand on this.

There are things I might be interested in including in my own course. One thing I would like to include, although in a very cursory way, is the problem of cultural evolution. I see it as an other type of evolution which has similarities and dissimilarities with biological evolution. I am doing a great deal of computer work on this and am fascinated by it (I consider it as a hobby however). I am interested in it also because I see great advantages in attacking it with a training in the theory of biological evolution. From the point of view of research, it would be important to secure the collaboration of some good cultural anthropologist. I am at the moment concentrating on African evolution because I know more about it; when in the States I might look at American Indians, applying there the same techniques I am working out for Africa, in collaboration with somebody who knows American Indians. The girl who wrote to you might be very interested in this sort of work and if she comes to Stanford you will be able to judge her; if she happens to come to Europe this summer you might suggest to her that she comes to visit me. There are still a number of problems here, and I am not quite sure yet as to the best time for my coming to Stanford this summer. If it is not at the end of July it is most likely to be in late October. By the way, I have not heard from Mike Durphy (could you ask Edna to tell him to write? He must be busy with exams right now but will be better off with time in a few days).

Thank you for the information on housing. I would like to receive regularly the bulletin of available houses, of which I have received the last issue. Can you give me an idea of the interest rate when borrowing money from banks? The loan available from the University does not cover much and the interest is fairly high. I hope that of banks is not much higher.

One point on the human biology program in general. A criticism which most Europeans voice against American culture is the lack of interest (in most school curricula) for "humanism". Would it not be important to encourage students of the human biology program to take up also some courses on the non-scientific side? I am not speaking of Psychology, Sociology, Economics, Cultural anthropology, which seem available in the program, at least to some extent. I am thinking of History of arts, History of literatures, History of science, Philosophy, and even Comparative religion (I hope at least Marguerite agrees on this). True, one cannot hope that students can take all these courses, but they should be encouraged to get some, especially those which are good. The idea is to hint at them that the approach "maximize efficiency and to hell with the rest" is not conducive to a balanced social life. I cam see that this talk may be difficult, and I am not a persuasive speaker. There may be (even too many) such courses at Menlo Free University. But it is important that people who would not go, spontaneously, to Menlo Free University have a chance to learn the taste of a "humanistic" approach in a more balanced and less casual way than MFU can offer.

I realize I am not using the word "humanism" properly but am at the moment unable to find a better one. What I am thinking about is perhaps summarized in the following. Let us simplify and consider the development of man through the last thousand years or so as follows: mysticism (the Middle Ages); aesthetism (the renaissance); rationalism (illuminism), efficientism (American pragmatism). Each of these —isms has shortcomings and severe limitations. We can probably achieve a better balance if we resist the strictly unilateral approach which each of these —isms symbolizes.

I had seen the paper on emotions and races. There are some racial differences in the paper, e.g. in the Melanesians. Tomkins has developed ways of quantitating the analysis of facial expressions. I had a talk recently with Goodenough (a co-worker of Witkin, both of them were here a week ago) who is doing something related to the project I had in mind and could supply us—by a simple addition to his setup—with video tapes of faces of people watching emotion-laden movies. So we may be able to make a very inexpensive start!

Yours.

luca

P.S.: As to the most purbate date for beginning mork in Stampard: January or February?